63. The composition of claim 59, wherein the anticancer agent is selected from the group consisting of adriamycin, vinblastin, and paclitaxel.

64. A method of treating cancer in a subject comprising:

administering a therapuetically effective amount of an epothilone to a subject in need thereof.

65. The method of claim 64, wherein the therapeutically effective amount of the epothilone is between about 0.001 mg/kg to about 40 mg/kg of body weight.

66. The method of claim 64, wherein the therapeutically effective amount of the epothilone is between about 0.01 mg/kg to about 40 mg/kg of body weight.

67. The method of claim 64, wherein the therapeutically effective amount of the epothilone is between about 0.001 mg/kg to about 25 mg/kg of body weight.

68. The method of claim 64, wherein the therapeutically effective amount of the epothilone is between about 0.01 mg/kg to about 25 mg/kg of body weight.

69. The method of claim 64, wherein the therapeutically effective amount of the epothilone is between about 0.001 mg/kg to about 10 mg/kg of body weight.

70. The method of claim 64, wherein the therapeutically effective amount of the epothilone is between about 0.01 mg/kg to about 10 mg/kg of body weight.

71. The method of claim 64, wherein the therapeutically effective amount of the epothilone is between about 0.001 mg/kg to about 1 mg/kg of body weight.

72. The method of claim 64, wherein the therapeutically effective amount of the epothilone is between about 0.01 mg/kg to about 1 mg/kg of body weight.

73. The method of claim 64, wherein the therapeutically effective amount of the epothilone is 25 mg/kg or greater of body weight.

74. The method of claim 64, wherein the therapeutically effective amount of the epothilone is between about 25 mg/kg to about 40 mg/kg of body weight.

75. The method of claim 64, wherein the therapeutically effective amount of the epothilone is effective to kill or inhibit the growth of tumor cells.

76. The method of claim 75, wherein the tumor cells are a solid tumor.

77. The method of claim 75, wherein the tumor cells are selected from the group consisting of breast cancer cells, melanoma cells, leukemia cells, and ovarian cancer cells.

78. The method of claim 77, wherein the leukemia cells are myelocytic, lymphocytic, acute, or chronic leukemic cells.

79. The method of claim 64, wherein the therapeutically effective amount of the epothilone is effective to kill or inhibit the growth of multidrug resistant cells.

80. A method of treating cancer in a subject comprising administering a therapeutically effective amount of a composition comprising an epothilone.

81. The method of claim 80, wherein said composition further comprises a pharmaceutically acceptable carrier or diluent.

82. The method of claim 80, wherein said composition is administered in combination with at least one cytotoxic agent.

83. The method of claim 82, wherein said at least one cytotoxic agent is an anticancer agent.

84. The method of claim 83, wherein said anticancer agent is selected from the group consisting of adriamycin, vinblastin, and paclitaxel.

85. A method for treating paclitaxel-resistant cancer comprising:

administering a therapeutically effective amount of an epothilone to a subject in need thereof, whereby said therapeutically effective amount of said epothilone is sufficient to kill or inhibit the growth of tumor cells resistant to paclitaxel.

86. A method for treating adriamycin-resistant cancer comprising:

administering a therapeutically effective amount of an epothilone to a subject in need thereof, whereby said therapeutically effective amount of said epothilone is sufficient to kill or inhibit the growth of tumor cells resistant to adriamycin.

87. A method of killing or inhibiting the growth of tumor cells comprising:

contacting tumor cells with an amount of a composition comprising an epothilone, effective to kill or inhibit the growth of tumor cells.

88. The method of claim 87, wherein said composition further comprises a pharmaceutically acceptable carrier or diluent.

89. The method of claim 87, wherein said composition is administered in combination with at least one cytotoxic agent.

90. The method of claim 89, wherein said at least one cytotoxic agent is an anticancer agent.

91. The method of claim 90, wherein said anticancer agent is selected from the group consisting of adriamycin, vinblastin, and paclitaxel.

92. The method of claim 87, wherein the tumor cells are a solid tumor.

93. The method of claim 87, wherein the tumor cells are selected from the group consisting

of breast cancer cells, melanoma cells, leukemia cells, and ovarian cancer cells.

94. The method of claim 93, wherein the leukemia cells are myelocytic, lymphocytic, acute or chronic leukemic cells.

95. The method of claim 87, wherein the effective amount of the epothilone is effective to kill or inhibit the growth of multidrug resistant cells.

In the specification:

On page 1, starting on line 27 and ending on line 34, please replace the paragraph with the following amended paragraph:

This application is a continuation of and claims priority under 35 U.S.C. § 120 to co-pending application number 09/874,514, filed June 5, 2001, which application is a continuation application of and claims priority under 35 U.S.C. § 120 to 08/986,025, filed December 3, 1997, now U.S. Patent No. 6,242,469, issued June 5, 2001, which claims priority under 35 U.S.C. § 119(e) to U.S. Provisional Application Serial Nos. 60/032,282, 60/033,767, 60/047,941, and 60/055,533, filed December 3, 1996, January 14, 1997, May 22, 1997, May 29, 1997, and August 13, 1997, respectively, the contents of which are hereby incorporated by reference into this application. This invention was made with government support under grants CA-28824, CA-39821, CA-GM 72231, CA-62948, and AI0-9355 from the National Institutes of Health, and grant CHE-9504805 from the National Science Foundation. Additionally, the present invention was supported in part by a fellowship from the United States Army to Dongfang Meng (DAMD 17-97-1-7146), and thus the government has certain rights in the invention.

On page 3, lines 21-22, please replace the paragraph with the following amended paragraph:

Figures 3(A) and 3(B) provide syntheses of key iodinated intermediates used to prepare hydroxymethylene- and hydroxypropylene-substituted epothilone derivatives.

On page 3, lines 24-27, please replace the paragraph with the following amended

paragraph:

Figures 3(C) and 3(D) provide methods of preparing hydroxymethylene- and hydroxypropylene-substituted epothilone derivatives, said methods being useful generally to prepare 12,13-*E* epothilones wherein R is methyl, ethyl, n-propyl, and n-hexyl from the corresponding *E*-vinyl iodides.

On page 3, lines 29-30, please replace the paragraph with the following amended paragraph:

Figures 3(E) and 3(F) show reactions leading to benzoylated hydroxymethyl-substituted desoxyepothilone and hydroxymethylene-substituted epothilone (epoxide).

On page 4, line 9, please replace the paragraph with the following amended paragraph:

Figures 6(A) and 6(B) provide a scheme of an olefin metathesis route to epothilone A and other analogues.

On page 4, line 29, please replace the paragraph with the following amended paragraph:

Figures 14(A) and 14(B) show the preparation of intermediate **4A**.

On page 5, lines 7-8, please replace the paragraph with the following amended paragraph:

Figures 18(A) and 18(B) provide a synthetic pathway to a protected intermediate for 8-desmethyl deoxyepothilone A.

On page 5, lines 10-11, please replace the paragraph with the following amended paragraph:

Figures 19(A), 19(B) and 19(C) provide a synthetic pathway to 8-desmethyl deoxyepothilone A, and structures of *trans*-8-desmethyl-desoxyepothiolone A and a trans-iodoolefin intermediate thereto.

On page 5, lines 13-22, please replace the paragraph with the following amended paragraph:

Figure 20(A) shows structures of epothilones A and B and 8-desmethylepothilone and Figure 20(B) shows a synthetic pathway to intermediate TBS ester **10** used in the preparation of desmethylepothilone A. (a) (*Z*)-Crotyl-B[(–)-Ipc]$_2$, –78°C, Et_2O, then 3N NaOH, 30% H_2O_2; (b) TBSOTf, 2,6-lutidine, CH_2Cl_2 (74% for two steps, 87% ee); (c) O_3, CH_2Cl_2/MeOH, –78°C, then DMS, (82%); (d) *t*-butyl isobutyrylacetate, NaH, BuLi, 0°C, then **6** (60%, 10:1); (e) $Me_4NBH(OAc)_3$, –10°C (50%, 10:1 α/β) or $NaBH_4$, MeOH, THF, 0°C, (88%, 1:1 α/β); (f) TBSOTf, 2,6-lutidine, –40°C, (88%); (g) Dess-Martin periodinane, (90%); (h) $Pd(OH)_2$, H_2, EtOH (96%); (I) DMSO, oxalyl chloride, CH_2Cl_2, –78°C (78%); (j) Methyl triphenylphosphonium bromide, NaHMDS, THF, 0°C (85%); (k) TBSOTf, 2,6-lutidine, CH_2Cl_2, rt (87%).

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On page 5, line 29, please replace the paragraph with the following amended paragraph:

Figures 22(A), 22(B) and 22(C) show a synthetic pathway to prepare epothilone analogue **27D.**

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On page 5, line 31, please replace the paragraph with the following amended paragraph:

Figures 23(A), 23(B) and 23(C) show a synthetic pathway to prepare epothilone analogue **24D.**

A13

On page 5, line 33, please replace the paragraph with the following amended paragraph:

Figures 24(A) and 24(B) show a synthetic pathway to prepare epothilone analogue **19D.**

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On page 5, line 35, please replace the paragraph with the following amended paragraph:

Figures 25(A), 25(B), 25(C) and 25(D) show a synthetic pathway to prepare epothilone

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A15 analogue **20D.**

On page 5, line 37, please replace the paragraph with the following amended paragraph:

Figures 26(A), 26(B), 26(C) and 26(D) show a synthetic pathway to prepare epothilone A16 analogue **22D.**

On page 6, lines 1-2, please replace the paragraph with the following amended paragraph:

Figures 27(A), 27(B) and 27(C) show a synthetic pathway to prepare epothilone analogue A17 12-hydroxy ethyl-epothilone.

On page 6, lines 4-7, please replace the paragraph with the following amended paragraph:

Figures 28(A) and 28(B) show the activity of epothilone analogues in a sedimentation test in comparison with DMSO, epothilone A and/or B. Structures 17-20, 22, and 24-27 are A18 shown in Figures 29-37, respectively. Compounds were added to tubulin (1mg/ml) to a concentration of 10 μM. The quantity of microtubules formed with epothilone A was defined as 100%.

On page 6, lines 30-32, please replace the paragraph with the following amended paragraph:

Figures 39(A) and 39(B) show epothilone A and epothilone analogues #1-7. Potencies A19 against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

On page 6, lines 34-36, please replace the paragraph with the following amended paragraph:

Figures 40(A) and 40(B) show epothilone B and epothilone analogues #8-16. Potencies A20 against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.